REMARKS/ARGUMENTS

I. Status of Claims

- Claims 21-23 and 33-35 remain pending for review.
- Claims 1-7, 10-13, and 31-32 are canceled.
- Claims 8-9, 14-20, and 24-30 are withdrawn.
- Claims 21 and 23 are currently amended.
- Claims 36-43 are new.
- Claim 21 is the only Independent Claim.
- Claims 31 and 32 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.
- Claims 21, 31-33, and 35 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Heller et al. (U.S. Patent No. 6,245,508 B1, June 12, 2001) (hereinafter **Heller**) in view of Goldstein et al. (U.S. Patent No. 4,584,075, Apr. 22, 1986) (hereinafter **Goldstein**).
- Claims 22 and 23 are rejected under 35 U.S.C. § 103(a) as being unpatentable over **Heller** in view of **Goldstein** as applied to claim 21 above, and further in view of Baselt (U.S. Patent No. 5,981,297, Nov. 9, 1999) (hereinafter referred to as **Baselt**).
- Claim 34 is rejected under 35 U.S.C. § 103(a) as being unpatentable over **Heller** in view of **Goldstein** as applied to claim 21 above, and further in view of Bier (U.S. Patent No. 4,040,940, Aug. 9, 1977) (hereinafter **Bier**).

II. Claim Amendments

Applicants amended Claims 21 and 23. Claim 21 now includes the limitation where the first semi-permeable membrane is positioned across a plurality of channels formed from wells of

a multi-well microplate. Support for this amendment can be found, for example, in paragraph [0173] of the Specification. See **Specification**, para. [0173].

Claim 23 now limits the particles to only magnetic particles. Applicants believe this amendment was necessary to conform to the January 16, 2009 election. Support can be found, for example, in paragraph [0074] of the Specification. See **Specification**, para. [0074].

Claims 36-43 are new. Claim 36 adds the limitation of deflecting bubbles with a frame having a porous membrane. Support can be found, for example, in paragraph [0219]. See **Specification**, para. [0219]. Claim 37 adds the limitation that the frame is placed at an angle of at about 30° to about 50° relative to the multi-well microplate. Support can be found, for example, in paragraph [0178]. Id.

Claim 38 adds the limitation of using glue to bind the first semi-permeable membrane to the first support and to bind the second semi-permeable membrane to the second support. Support can be found, for example, in paragraphs [0212] and [0219]. See **Specification**, paras. [0212] and [0219]. Claim 39 adds the further limitation that the glue is octylcyanoacrylate glue. Support can be found, for example, in paragraph [0212]. Id. at para. [0212]. Claim 40 adds the further limitation that the glue is cyanoacrylate glue. Support can be found, for example, in paragraph [0219]. Id. at para. [0219].

Claim 41 adds the limitation that the surface layer is activated with plasma. Support can be found, for example, in paragraphs [0225]-[0231]. See **Specification**, paras. [0225]-[0231]. Claim 42 adds the limitation that the surface layer is activated by hydrophobization. Support can be found, for example, in paragraphs [0232]-[0233]. Id. at paras. [0232]-[0233].

Claim 43 reintroduces the elected species centrifugal force of canceled Claim 7. See Response to Restriction Requirement (dated Dec. 12, 2007), p. 2, para. 2. It appears Applicants

inadvertently left out this limitation when previously amending the claims. Support can be found, for example, in paragraph [0074] of the Specification. See **Specification**, para. [0074].

III. Response

A. Section 112, first paragraph of 35 U.S.C. is now overcome.

Examiner rejected Claims 31 and 32 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. See Office Action (dated 04/27/2009), pp. 6-7.

In response, Applicants canceled Claims 31 and 32. This action renders these rejections moot. Therefore, Applicants respectfully request Examiner to withdraw these rejections.

B. The amended and new claims appear to overcome the cited prior art.

Examiner stated that combining **Heller** with **Goldstein** makes Claims 21, 31-33, and 35 unpatentable. See Office Action (dated 04/27/2009), pp. 8-13. As for Claims 22 and 23, Examiner stated they are also unpatentable when **Heller** and **Goldstein** are combined with **Baselt**. Id. at 14-15. As for Claim 34, Examiner stated that it is unpatentable when **Heller** and **Goldstein** are combined with **Bier**. Id. at 15-17.

In response, Applicants have amended the claims to provide additional limitations, as seen in the **Amendments to the Claims**. See supra § **Amendments to the Claims**. With these amendments, Applicants believe the cited prior art, when combined, do not recreate the claimed invention.

Referring to Claims 21 and 36-37, the limitations focus on deflecting bubbles with a frame having a porous membrane that can be placed at an angle of at about 30° to about 50° relative to a multi-well microplate. See supra, § **Amendments to the Claims**; see also **Specification**, para. [0219]. As taught in the Specification, it is expected that bubbles will form and accumulate. See **Specification**, paras. [0173]-[0174] and [0219]. To prevent bubbles from

accumulating on the electrophoretic plate, Applicants insert an optional frame with a porous membrane (sometimes referred to as a bubble deflector). Id. The optional bubble deflector is expected to deflect bubbles to the chamber wall. Id. Such deflector can be seen as illustrated in Figure 8. See **Specification**, Fig. 8. As a further limitation, where the optional bubble deflector is inserted, it is to be inserted at an angle of about 30°-50° relative to the multi-well microplate. Id. at para. [0178].

None of the prior art speaks to these additional limitations. Of the named prior art, only **Heller** and **Bier** come close.

Heller teaches using mesh type permeation layers, such as an acrylamide-based permeation layer, to raise the maximum accessible current density before bubbles form due to water hydrolysis. See **Heller**, col. 18, ll. 7-21 and 56-65. Furthermore, by attaching capture probes, such as DNA capture probes, onto the permeation layer, **Heller** provides a means of special functionality attachment to the surface of the permeation layer. Id. at col. 18, ll. 36-41.

However, these are the only concerns (maximizing current density and providing special functionality attachment sites) of **Heller**. Nowhere could Applicants find where **Heller** speaks to using such permeation layer to protect the electrophoretic plate from the accumulation of bubbles.

Similarly, **Bier** does not prevent bubble accumulation like Applicants' claimed invention. In particular, **Bier** teaches a rotating seal fraction collector assembly **26**. See **Bier**, col. 4, ll. 63-67. The two mating surfaces **29, 33** of the rotating seal fraction collector assembly **26** must be wetted by an eluting buffer or lubricant to prevent an air bubble from entering into the electrophoresis channel. Id. **Bier** goes on to state that for this purpose, regulating hydrostatic pressure in the efferent tube **11** may be necessary. Id. at col. 4, l. 67 – col. 5, l. 2.

While **Bier** attempts to prevent bubble accumulation in this way, **Bier's** technique is not the same as Applicants' claimed technique. First, **Bier's** component is a seal fraction collector assembly that rotates. In other words, it is a round device that rotates. Applicants' version is flat, as illustrated in Figure 8. See, e.g., **Specification**, Fig. 8. Second, the mating surfaces of the seal fraction collector assembly must be lubricated. In contrast, the surface of Applicants' bubble deflector does not use lubrication.

Moreover, as another distinction, Applicants have their bubble deflector at an angle relative to a multi-well microplate. See supra. This further limitation is neither seen in **Heller** nor **Bier**.

Referring to Claims 21 and 38-40, the limitations focus on the type of binding. In particular, Applicants claim using glue to bind the first semi-permeable membrane to the first support and to bind the second semi-permeable membrane to the second support. In one embodiment, the glue is octylcyanoacrylate glue. See, e.g., **Specification**, para. [0212]. In another embodiment, the glue is cyanoacrylate glue (such as "crazy glue"). See, e.g., **Specification**, para. [0219].

In some cases, it may be helpful to use octylcyanoacrylate glue as a way of avoiding two major drawbacks of cyanoacrylate glue. See **Specification**, para. [0212]. In one instance, cyanoacrylate glue tends to be highly volatile. Id. In another instance, blooming may occur. Id. (indicating that blooming refers to the glue being deposited on an unprotected film). Yet, while octylcyanoacrylate glue has these advantages, cyanoacrylate glue can suffice at times as well.

In any event, none of the cited prior refers to using glue, octylcyanoacrylate glue, or cyanoacrylate glue to bind a membrane to a support.

Referring to Claims 21, 33, and 41-42, the limitations focus on activation of the surface layer. In one embodiment, the claimed invention states that the surface layer is activated by plasma. See **Specification**, paras. [0225]-[0231]. In another embodiment, the claimed invention states that the surface layer is activated by hydrophobization. See **Specification**, paras. [0232]-[0233]. Neither activation by plasma nor hydrophobization are taught in any of the cited prior art.

Examiner believes that **Heller** teaches that the surface layer is an activated surface. See Office Action (dated 04/27/2009), para. 1 (suggesting that **Heller's** functionalized surface as pointed out in **Heller's** col. 18, ll. 7-17 equates to Applicants' activated surface). Yet, it appears that **Heller** lacks some of Applicants' teachings. In particular, **Heller** teaches that the micro-locations were created on the permeation layer. See **Heller**, col. 18, ll. 7-17. The surface of these micro-locations (as well as the polymer layers over the micro-locations) was then chemically modified to create specialized attachment sites for surface functionality. Id. However, **Heller** does not reveal using plasma or hydrophobization to activate the surface layer.

Applicants also reviewed **Goldstein**, **Baselt**, and **Bier** to see if these prior art taught using plasma or hydrophobization. None of them appear to do so. **Goldstein** discloses using activation agents to treat Barrier 3 (an anion-selective membrane having a macroreticular surface). See **Goldstein**, col. 3, ll. 45-51, col. 9, ll. 53-57. **Goldstein** states that the activation agents used are generally those known in the art, such as "cyanogen bromide, trichloro-s-triazine, isocyanate, glutaraldehyde, and the like as appropriate to the barrier material and the desired ligand." Id. at col. 3, ll. 45-51. However, nowhere does **Goldstein** use plasma or hydrophobization.

As for **Baselt**, **Baselt** talks about activating a magnetic filed detector, which is a microfabricated device bearing magnetoresistive elements. See **Baselt**, col. 5, ll. 35-36, col. 7, ll. 6-8. This detector is a device. There is no mentioning of plasma or hydrophobization here.

As for **Bier**, there is no mentioning of activation, plasma, or hydrophobization at all.

Referring to Claims 21-23 and 43, the limitation focuses on the particles as magnetic particles that can be moved using centrifugal forces. Support can be found, for example, in paragraphs [0136]-[0143] and [0251]. See **Specification**, paras. [0136]-[0143] and [0251].

Like above, none of the prior art speak to these additional limitations. Of the named prior art, only **Heller** and **Bier** barely mentions the use of centrifugal forces.

Heller generally speaks to separating DNA from cellular debris using centrifugation. See **Heller**, col. 2, ll. 33-35. **Bier** mentions that a combination of centrifugal field and an electrical field may be used to enhance electrophoretic separation. See **Bier**, col. 1, ll. 60-64. However, that's it. Neither **Heller** nor **Bier** teach Applicants' additional limitation of using centrifugal forces to move magnetic particles.

Because of these differences, Applicants believe these additional limitations overcome the cited prior art combinations. Hence, Applicants respectfully request Examiner to withdraw these §103 rejections.

C. Dependent Claims 22-23 and 33-43 depend on Independent Claim 21.

Because Dependent Claims 22-23 and 33-43 ultimately depend on Independent Claim 21, the arguments presented for the independent claim also apply to these dependent claims. Therefore, Applicants respectfully request withdrawal of these rejections as well.

IV. Conclusion

If Examiner agrees with Applicants' above arguments and Examiner's next prior art search does not result in any prior art that can be used to reject the amended claims, Applicants believe the amended independent claim and all their dependent claims would be in condition for allowance. In such event, Applicants respectfully request Examiner to allow the amended claims.

Should there are any outstanding issues that might be resolved by an interview or an Examiner's Amendment, Applicants request that the Examiner call the Applicants' agent at the telephone number shown below.

V. Deposit Account

Applicants hereby authorize the Commissioner to credit or debit any outstanding fees in connection with this patent application using Deposit Account No. 50-3212.

Respectfully submitted,

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Date: August 27, 2009

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